PARTITIONING OF EU(III) COORDINATION COMPLEXES INTO LIPID BILAYER

A.V.Yudintsev[1], V.M.Trusova[1], G.P.Gorbenko[1], T.Deligeorgiev[2], A.Vasilev[2]
[1]*V.N. Karazin Kharkov National University, 4 Svobody Sq., Kharkov, 61077*
[2]*Department of Applied Organic Chemistry, Faculty of Chemistry, University of Sofia, Bulgaria*
Received 15 October, 2007

The present study is focused on development of liposomal delivery systems for two newly synthesized drugs with high anticancer activity – Eu(III) coordination complexes, referred to as V3 and V4. These pharmacological preparations belong to a new class of antineoplastic drugs, whose high cytotoxic potential has been demonstrated very recently. Liposomes composed of phosphatidylcholine (PC) were chosen as effective nanocarriers due to their undisputable advantages such as enhanced drug solubility, reduced toxicity, improved stability, etc. The results of preformulation studies are presented, describing UV absorption spectroscopy-based evaluation of the degree of drug loading into liposomes which strongly determines the therapeutic and toxic effects of the pharmacological compounds. Drug association with the lipid bilayer was followed by the absorbance increase with maximum position being independent on lipid concentration. Zwitterionic nature of PC and relatively high hydrophobicity of the pharmaceuticals allowed us to conclude that drug-lipid binding is governed preferentially by hydrophobic interactions. Higher efficiency of encapsulation into the lipid bilayers was found for V3 ($K_p = 1.4 \times 10^5$) compared to V4 ($K_p = 6.7 \times 10^3$). This effect was interpreted in terms of V3 influence on bilayer molecular organization giving rise to facilitated partitioning of this drug into the vesicle interior.

KEY WORDS: partition coefficient, Eu(III) coordination complexes, drug-lipid interactions